Original Article The therapeutic effect of the digestive endoscopy tunneling technique on upper gastrointestinal muscularis propria tumors

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Abstract: Objective: To analyze the therapeutic effect of digestive endoscopy tunneling technology on upper gastrointestinal muscularis propria tumors. Methods: A total of 120 patients with upper gastrointestinal tumors in the muscularis propria treated in our hospital in the past two years were recruited as the study cohort. They were treated using the digestive endoscopic tunneling technique, specifically, endoscopic submucosal tunneling tumor resections, and their clinical data, surgical conditions, pathological results, incidences of complications (CR), and anxiety scores were recorded. A postoperative follow-up was conducted on the patients. Results: A total of 122 tumors were removed from 120 patients, including two patients who had two tumors each. The largest diameter among the tumors was 4.2 cm, and the average diameter was (2.01±1.56) cm. There were 86 tumors located in the superficial layer of the muscularis propria and 36 pieces in the deep layer. No significant differences were found in the patients' clinical data (P > 0.05). The 120 patients all successfully completed their operations. The operation times ranged between 26 min and 158 min. The en bloc resection rate was 95.8%, and the average postoperative hospital stay was 3.8 days. The pathological diagnoses showed that there were 72 leiomyomas, accounting for 59.0% of the total, and 44 stromal tumors, accounting for 36.1%. There were 2 glomus tumor cases, accounting for 1.6%, and 4 nerve sheath tumor cases, accounting for 3.3%. No patient had delayed gastrointestinal bleeding or mucosal perforations. The probability of subcutaneous emphysema and pneumothorax was 1.7%, the probability of pneumoperitoneum was 0.8%, the probability of retrosternal pain was 10.0%, and the total incidence of CR was 14.2%. No tumor recurrence or residual phenomenon was found at the 3, 6, or 12 month follow ups after the treatment, and the patients' satisfaction rate was as high as 98.3%. Their anxiety scores also decreased significantly over time (P < 0.001). Conclusion: Digestive endoscopy tunnel technology can effectively improve the surgical success rate of patients with upper gastrointestinal muscularis propria tumors, reduce the probability of CR, and reduce patients' psychological pressure. It has significant effects in the treatment of upper gastrointestinal muscularis propria tumors and should be widely applied in clinical practice.

Keywords: Digestive endoscopy tunnel technique, upper gastrointestinal tract, muscularis propria tumors, curative effect analysis

Introduction

Upper gastrointestinal tumor to the muscularis propria is a type of submucosal tumor (SMT), which are generally located at a deeper level. Some of them have the possibility of malignant transformation, and it is difficult to make an accurate diagnosis before surgery. Therefore, determining how to carry out a more efficient and convenient treatment for SMT of the muscularis propria has always been a focus of practical exploration. At present, the commonlyused treatment methods for the disease clinically are follow-up observation and surgery, both of which have their own limitations: followup observations tend to aggravate the patients' psychological burdens, and there is the possibility of delaying the treatment timing. Surgery is likely to cause major trauma to patients and increase the probability of complications, so it is unfavorable for the subsequent recovery of patients [1-3]. In recent years, with the further

development of endoscopic tunneling technology, peroral endoscopic myotomy (POEM) took the lead and was widely applied. In addition, digestive endoscopy tunneling technology can finally be applied in the treatment of SMT in the upper gastrointestinal muscularis propria. Submucosal tunneling endoscopic resection (STER) has emerged. This technique enables a minimally invasive treatment for patients by establishing staggered entry and exit incisions, which can not only achieve a complete resection of SMT of the muscularis propria, but also has the advantages of fewer complications and a faster recovery [4-7]. In order to explore the therapeutic effect of digestive endoscopy tunneling technology on SMT in upper gastrointestinal muscularis propria, 120 patients with related diseases admitted to our hospital in the past two years were selected for this study. The results are as follows.

Materials and methods

General patient information

In total, 120 SMT patients admitted to our hospital in the past two years were recruited as the study cohort, all of whom were between 28 and 65 years old, and the cohort included 65 male patients and 55 female patients. No significant differences were found in the general patient clinical data, such as age or course of the disease (P > 0.05), enabling them to serve as the study cohort.

Inclusion criteria

The inclusion criteria were: ① Patients confirmed to have SMT of the upper gastrointestinal proper muscularis propria. ② Patients without a high risk of malignant tumors. ③ The patients or their families signed the informed consent form. ④ This study was approved by our hospital's ethics committee.

Exclusion criteria

The exclusion criteria were: ① Patients who were pregnant or lactating. ② Patients with a clotting disorder or other serious illness. ③ Patients with a high risk of malignant tumors.
④ Patients with mental disorders or who were unable to communicate with the researchers.

Methods

Surgical methods

All the patients were treated with antibiotics before surgery, and the STER therapy was used under general anesthesia. (1) Establishment of the tunnel entrance: The tumor was located by placing a transparent cap (Olympus) at the front end of the gastroscope (Type 260 Gastroenteroscopy system, Japan). The mucosa at 4 cm near the mouth was injected (90 ml normal saline, 0.9 ml epinephrine, and 2 ml indigo carmine were mixed). It was cut longitudinally using a high-frequency electric knife for more than 1.5 cm and was separated 0.5 cm laterally along the submucosa. 2 SMT excision of the muscularis propria: The tunnel was separated from the tunnel entrance along the submucosal layer to establish a submucosal tunnel and expose the tumor. The intrinsic muscularis and tissues around the tumor were separated to ensure the integrity of the capsule, and the tumor was completely stripped and removed. If a gastric SMT tumor was tightly adhered to the serous membrane and could not be removed directly, then the serous membrane was cut along the tumor with a Hybrid knife (ERBE Co., Ltd.) and the serous membrane was removed. After removing the tumor, normal saline was used to flush the tunnel and stop the bleeding. The excess fluid inside was sucked out, and several metal patches were inserted into the mucosal layer to make the incision. The lesions were flushed with a neutral formaldehyde solution and sent for examination to obtain the pathological results [8-11].

Postoperative management

All the patients fasted for 1 day after the surgery. If there were no abnormalities on the second day, 4 days of liquid diet could be administered, and the transition to a normal diet could be made gradually within 14 days. If the patient has pneumoperitoneum, then an abdominal puncture needle was used to treat the condition. The patients with pneumothoraxes were fitted with a closed thoracic drainage flask to facilitate lung tissue expansion. The patients were observed to determine whether they had other symptoms, and they received conventional antibiotics, hemostasis, or other treatment measures [8, 12-14]. The digestive endoscopy tunneling technique and upper gastrointestinal tumors

Group	Male	Female	t/χ²	P 0.329	
Average age	40.21±5.60	41.23±5.30	0.981		
Tumor site			2.12	0.145	
Esophagus	51	40			
Cardia	11	12			
Greater curvature of stomach antrum	3	2			
Lesser curvature of stomach	2	1			
Muscularis propria			0.287	0.592	
Superficial layer	45	41			
Deep layer	21	15			
Tumor size (cm)			0.763	0.383	
≤2	35	29			
> 2 and ≤3.5	28	26			
> 3.5	2	2			

Table 1. Comparison of the clinical data

Post-operative follow-up

Endoscopic examinations were performed on the patients at 3, 6, and 12 months after their operations, and once a year thereafter, to observe the wound healing and any residual or recurrence of the lesion tissue.

Outcome measures

1) Clinical data: The information includes age, gender, tumor location, source level, tumor size, and so on. 2 Surgical condition: Including the success rate of the surgery, the operation time, the whole section removal rate, the postoperative hospital stay, and other information. ③ The pathological results: there were leiomyoma, stromal tumor, glomus tumor, and schwannoma cases, and their proportions were calculated. ④ CR: The subcutaneous hematoma, pneumothorax, pneumoperitoneum, delayed gastrointestinal bleeding (DGB), poststernal pain, and mucosal perforation rates were calculated respectively. (5) Postoperative follow-up: any recurrence or residual signs of the tumors were investigated, and the treatment satisfaction was rated. The follow-up times were 3, 6, and 12 months after the operations. 6 Anxiety scores: The calculated anxiety scores ranged from 0 points to 100 points, and the higher the score was, the more anxious the patient was. The times the anxiety scores were determined were before and after the operations, and the investigation times after the operation were the same as the follow-up times.

Statistical analysis

SPSS 20.0 software was used to process the data, and GraphPad Prism 7 (GraphPad Software, San Diego, USA) was used for the image rendering in this research. The research included enumeration and measurement data, which were examined using X^2 and t tests. P < 0.05 was considered statistically significant.

Results

Clinical data

A total of 122 tumors were removed from 120 patients, including 1 patient with a tumor in the esophagus and the cardia, 1 patient with a tumor in the greater curvature of the gastric antrum and the cardia. The largest tumor had a diameter of 4.2 cm, and the average size was (2.01 ± 1.56) cm. There was no significant difference in the patients' general clinical data (P > 0.05). See **Table 1**.

Surgical conditions

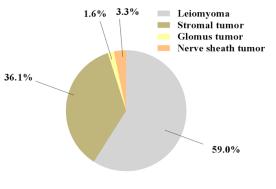
All the patients successfully completed the operations, and the operation times ranged from 26 to 158 min, and the whole block removal rate was 95.8% (115/120). The post-operative hospital stays were up to 5 days. See **Table 2**.

Pathological results

In total, 72 leiomyomas, 44 stromal tumors, and 6 glomus tumors and neurilemmoma were

Table 2. Comparison of the patients' operations

Group	Male (n=65)	Female (n=55)	X ²	Ρ
Operation Success Rate (%)	100 (65/65)	100 (55/55)	< 0.001	1.000
Duration (min)	64.00±2.30	63.90±2.50	0.218	0.828
whole block removal rate (%)	95.4 (62/65)	96.4 (53/55)	0.072	0.789
postoperative hospital stay (d)	3.81±0.20	3.79±0.30	0.411	0.681



Pathological results

Figure 1. Analysis of the patients' pathological results. Note: In **Figure 1**, the gray area represents leiomyomas, the green area represents stromal tumors, the yellow area represents glomus tumors, and the orange area represents nerve sheath tumors. There were 72 leiomyomas, accounting for 59.0%, 44 stromal tumors (36.1%), 2 glomus tumors (1.6%), and 4 nerve sheath tumors (3.3%).

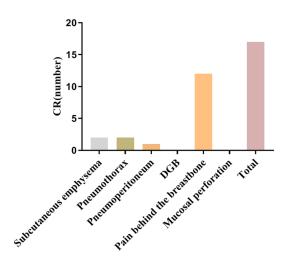


Figure 2. Comparison of the CR data. Note: **Figure 2** shows subcutaneous emphysema, pneumothorax, pneumoperitoneum, delayed gastrointestinal bleeding, retrosternal pain, mucosal perforations, and the total cases from left to right on the horizontal axis. There were 2 cases of subcutaneous emphysema, 2 cases of pneumothorax, 1 case of pneumoperitoneum, 0 cases of delayed gastrointestinal hemorrhage and mucosal perforation, and 12 cases of retrosternal pain.

confirmed by routine pathological diagnosis in the 122 samples. See **Figure 1**.

The incidence of delayed gastrointestinal bleeding and mucosal perfora-

tion was 0.0%. The incidence of subcutaneous emphysema and pneumothorax was 1.7%. The incidence of pneumoperitoneum was 0.8%, and the incidence of retrosternal pain was 10.0%. The total CR was 14.2%. See **Figure 2**.

Post-operation follow-up

In the follow-ups at 3 months, 6 months, and 12 months, no recurrence or residuals were found. The treatment satisfaction rate was as high as 98.3%. See **Table 3**.

Anxiety scores

Before the treatment, and at 3 months after the treatment, 6 months after the treatment, and 12 months after the treatment, the anxiety scores were (80.21 ± 11.29), (75.21 ± 12.45), (58.33 ± 14.19) and (21.52 ± 13.33), respectively. The anxiety scores of the 120 patients were significantly decreased with time (P < 0.001). See **Figure 3**.

Discussion

SMT of the upper gastrointestinal proper muscle-layer mainly consists of leiomyoma, stromal tumors, and schwannoma. With the continuous upgrading of endoscopic techniques, the detection rate of SMT has been increasing yearly, and it has become a common disease affecting human life. At present, the common treatment for this disease mainly includes follow-up observations and surgical resection. A part of the intrinsic muscle layer. SMT has the possibility of malignant transformation, and the follow-up observations are likely to delay the disease and aggravate the patients' psychological burdens, so surgical resection has become the preferred treatment. Surgical resection can also be divided into surgical operations and endoscopic treatment, among which surgical operation has the inherent disadvantages of greater trauma, and it can easily increase the incidence of complications in pa-

Group	Cases	Ratio (%)	X ²	Р			
Recurrence							
Yes	0	0.0					
No	120	100.0					
Residual							
Yes	0	0.0					
No	120	100.0					
Treatment satisfaction			224.267	< 0.001			
Very satisfied	82	68.3					
Satisfied	36	30.0					
Dissatisfied	2	1.7					

 Table 3. Patients with tumor recurrences and residuals and the treatment satisfaction

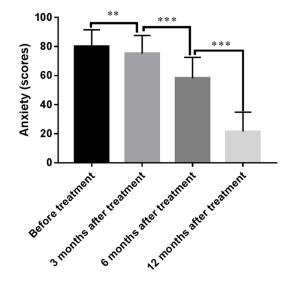


Figure 3. Comparison of the anxiety scores before and after STER. Note: In Figure 3, from left to right, the horizontal axis represents before the treatment, 3 months after the treatment, 6 months after the treatment, and 12 months after the treatment. The anxiety scores were (80.21 ± 11.29), (75.21 ± 12.45), (58.33 ± 14.19) and (21.52 ± 13.33) before the treatment, 3 months after the treatment, 6 months after the treatment, and 12 months after the treatment. * indicates P < 0.001.

tients and is unfavorable to their postoperative recovery. Therefore, it is vital to expand the exploration and practice of endoscopic treatment as it has less trauma in clinical practice [15-18]. After Inone et al. applied POEM to achalasia of the esophagus and cardia, endoscopic tunneling technology has obtained practical experience in the field of upper gastrointestinal proper muscularis disease, and then STER technology for SMT treatment of upper gastrointestinal proper muscularis emerged. This treatment method not only has the advantages of fewer complications and a faster recovery, it can also reduce the psychological burdens of cancer patients, so it is extremely beneficial for the SMT treatment of the upper digestibility intrinsic muscle layer [19-21]. Although it was generally believed that STER is limited to treating tumors with a maximum diameter of 3.5 cm, four tumors with diameters of more than 3.5 cm were successfully removed in this study, proving that this technique has a broader application.

In addition, among the 122 tumors resected in this study, the maximum diameter was 4.2 cm, and the average diameter was (2.01±1.56) cm. A total of 86 tumors were located in the superficial layer of the musculus propria. At the follow-ups of 3, 6, and 12 months after the treatment, no tumor recurrence or residual was found in the patients, and the treatment satisfaction rate was as high as 98.3%. The anxiety scores also decreased significantly over time (P < 0.001). The above data show that STER has a good effect in treating SMT in the upper gastrointestinal muscularis propria and has a low incidence of complications and brings a significant reduction in the patients' psychological burdens. However, Zaheer Nabi et al. [22] calculated the overall resection rate, the incidence of adverse events, and the recurrence probability of patients who underwent STER therapy for muscularis propria tumors over 1.0 cm in the upper digestive tract, and they concluded that the overall resection rate was 97.7%, the incidence of adverse events was 15.9%, and the recurrence rate was 0.0%. The results of this study are consistent with the results obtained in this paper. It was confirmed that digestive endoscopy tunneling technology is effective for the SMT treatment of upper gastrointestinal musculus propria.

To sum up, the digestive endoscopic tunneling technique represented by STER has a significant effect in treating SMT musculus propria tumors of the upper digestive tract and should be widely applied in clinical practice.

Disclosure of conflict of interest

None.

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References

- [1] Kamata K, Takenaka M, Kitano M, Omoto S, Miyata T, Minaga K, Yamao K, Imai H, Sakurai T, Watanabe T, Nishida N, Chikugo T, Chiba Y, Imamoto H, Yasuda T, Lisotti A, Fusaroli P and Kudo M. Contrast-enhanced harmonic endoscopic ultrasonography for differential diagnosis of submucosal tumors of the upper gastrointestinal tract. J Gastroenterol Hepatol 2017; 32: 1686-1692.
- [2] Lee CM and Park S. Laparoscopic techniques and strategies for gastrointestinal GISTs. J Vis Surg 2017; 3: 62.
- [3] He G, Wang J, Chen B, Xing X, Wang J, Chen J, He Y, Cui Y and Chen M. Feasibility of endoscopic submucosal dissection for upper gastrointestinal submucosal tumors treatment and value of endoscopic ultrasonography in pre-operation assess and post-operation follow-up: a prospective study of 224 cases in a single medical center. Surg Endosc 2016; 30: 4206-13.
- [4] Jain D, Desai A, Mahmood E and Singhal S. Submucosal tunneling endoscopic resection of upper gastrointestinal tract tumors arising from muscularis propria. Ann Gastroenterol 2017; 30: 262-272.
- [5] Yeung B, Chiu P, Teoh A, Zheng L, Chan S, Lam K, Tang R and Ng EK. An innovative ex-vivo porcine upper gastrointestinal model for submucosal tunnelling endoscopic resection (STER). Endosc Int Open 2016; 4: E1101-E1106.
- [6] Kishiki T, Lapin B, Wang C, Jonson B, Patel L, Zapf M, Gitelis M, Cassera MA, Swanström LL and Ujiki MB. Teaching peroral endoscopic myotomy (POEM) to surgeons in practice: an "into the fire" pre/post-test curriculum. Surg Endosc 2018; 32: 1414-1421.
- [7] Martinek J, Svecova H, Vackova Z, Dolezel R, Ngo O, Krajciova J, Kieslichova E, Janousek R, Pazdro A, Harustiak T, Zdrhova L, Loudova P, Stirand P and Spicak J. Per-oral endoscopic myotomy (POEM): mid-term efficacy and safety. Surg Endosc 2018; 32: 1293-1302.
- [8] Du C and Linghu E. Submucosal tunneling endoscopic resection for the treatment of gastrointestinal submucosal tumors originating from the muscularis propria layer. J Gastrointest Surg 2017; 21: 2100-2109.
- [9] Marcella C, Shi R, Yu T, Sarwar S, Wang X and Liu Y. Asymptomatic esophageal glomus tu-

mor: case report. J Gastrointest Oncol 2019; 10: 1015-1020.

- [10] Dellatore P, Bhagat V and Kahaleh M. Endoscopic full thickness resection versus submucosal tunneling endoscopic resection for removal of submucosal tumors: a review article. Transl Gastroenterol Hepatol 2019; 4: 45.
- [11] Gluzman MI, Kashchenko VA, Karachun AM, Orlova RV, Nakatis IA, Pelipas IV, Vasiukova EL, Rykov IV, Petrova VV, Nepomniashchaia SL and Klimov AS. Technical success and short-term results of surgical treatment of gastrointestinal stromal tumors: an experience of three centers. Transl Gastroenterol Hepatol 2017; 2: 56.
- [12] Tsuji Y, Kusano C, Gotoda T, Itokawa F, Fukuzawa M, Sofuni A, Matsubayashi J, Nagao T, Itoi T and Moriyasu F. Diagnostic potential of endoscopic ultrasonography-elastography for gastric submucosal tumors: a pilot study. Dig Endosc 2016; 28: 173-8.
- [13] ASGE Technology Committee, Aslanian HR, Sethi A, Bhutani MS, Goodman AJ, Krishnan K, Lichtenstein DR, Melson J, Navaneethan U, Pannala R, Parsi MA, Schulman AR, Sullivan SA, Thosani N, Trikudanathan G, Trindade AJ, Watson RR and Maple JT. ASGE guideline for endoscopic full-thickness resection and submucosal tunnel endoscopic resection. Video-GIE 2019; 4: 343-350.
- [14] Peng W, Tan S, Huang S, Ren Y, Li H, Peng Y, Fu X and Tang X. Efficacy and safety of submucosal tunneling endoscopic resection for upper gastrointestinal submucosal tumors with more than 1-year' follow-up: a systematic review and meta-analysis. Scand J Gastroenterol 2019; 54: 397-406.
- [15] Shibasaki S, Suda K, Obama K, Yoshida M and Uyama I. Should robotic gastrectomy become a standard surgical treatment option for gastric cancer? Surg Today 2020; 50: 955-965.
- [16] Guo Y, Jing X, Zhang J, Ding X, Li X, Mao T and Tian Z. Endoscopic removal of gastrointestinal stromal tumors in the stomach: a single-center experience. Gastroenterol Res Pract 2019; 2019: 3087298.
- [17] Na HK, Ahn JY, Lee JH, Jung KW, Kim DH, Choi KD, Song HJ, Lee GH and Jung HY. Clinical outcomes of endoscopic treatment for gastric epithelial neoplasm in remnant stomach after distal gastrectomy. Dig Liver Dis 2019; 51: 675-680.
- [18] Chen H, Li B, Li L, Vachaparambil CT, Lamm V, Chu Y, Xu M and Cai Q. Current status of endoscopic resection of gastric subepithelial tumors. Am J Gastroenterol 2019; 114: 718-725.
- [19] Parsa N and Khashab MA. POEM in the treatment of esophageal disorders. Curr Treat Options Gastroenterol 2018; 16: 27-40.

- [20] Teitelbaum EN, Dunst CM, Reavis KM, Sharata AM, Ward MA, DeMeester SR and Swanström LL. Clinical outcomes five years after POEM for treatment of primary esophageal motility disorders. Surg Endosc 2018; 32: 421-427.
- [21] Werner YB and Rösch T. POEM and submucosal tunneling. Curr Treat Options Gastroenterol 2016; 14: 163-77.
- [22] Nabi Z, Ramchandani M, Sayyed M, Darisetty S, Kotla R, Rao GV and Reddy DN. Outcomes of submucosal tunneling endoscopic resection in upper gastrointestinal sub-epithelial tumors. Indian J Gastroenterol 2019; 38: 509-517.